



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Kenneth C. Cundy et al.

Application No.: 09/974,768

Filing Date: October 9, 2001

Title: BILE-ACID CONJUGATES FOR PROVIDING SUSTAINED SYSTEMIC CONCENTRATIONS OF DRUGS

Group Art Unit: 1616

Examiner: BARBARA P BADIO

Confirmation No.: 6895

AMENDMENT/REPLY TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Enclosed is a reply for the above-identified patent application.

☐ A Petition for Extension of Time is also enclosed.

☐ Terminal Disclaimer(s) and the ☐ \$65.00 (2814) ☐ \$130.00 (1814) fee per Disclaimer due under 37 C.F.R. § 1.20(d) are also enclosed.

☐ Also enclosed is/are _____

☐ Small entity status is hereby claimed.

☐ Applicant(s) requests continued examination under 37 C.F.R. § 1.114 and enclose the ☐ \$395.00 (2801) ☐ \$790.00 (1801) fee due under 37 C.F.R. § 1.17(e).

☐ Applicant(s) requests that any previously unentered after final amendments not be entered. Continued examination is requested based on the enclosed documents identified above.

☐ Applicant(s) previously submitted _____

on _____
for which continued examination is requested.

☐ Applicant(s) requests suspension of action by the Office until at least _____, which does not exceed three months from the filing of this RCE, in accordance with 37 C.F.R. § 1.103(c). The required fee under 37 C.F.R. § 1.17(i) is enclosed.

☐ A Request for Entry and Consideration of Submission under 37 C.F.R. § 1.129(a) (1809/2809) is also enclosed.

- ☒ No additional claim fee is required.
- ☐ An additional claim fee is required, and is calculated as shown below.

| AMENDED CLAIMS | | | | | |
|--|---------------|---|--------------|---------------------|----------------|
| | No. of Claims | Highest No. of Claims Previously Paid For | Extra Claims | Rate | Additional Fee |
| Total Claims | | MINUS = | 0 | x \$50.00 (1202) = | \$ 0.00 |
| Independent Claims | | MINUS = | 0 | x \$200.00 (1201) = | \$ 0.00 |
| If Amendment adds multiple dependent claims, add \$360.00 (1203) | | | | | |
| Total Claim Amendment Fee | | | | | \$ 0.00 |
| <input type="checkbox"/> Small Entity Status claimed - subtract 50% of Total Claim Amendment Fee | | | | | \$ 0.00 |
| TOTAL ADDITIONAL CLAIM FEE DUE FOR THIS AMENDMENT | | | | | \$ 0.00 |

- ☐ A check in the amount of _____ is enclosed for the fee due.
- ☐ Charge _____ to Deposit Account No. 02-4800.
- ☐ Charge _____ to credit card. Form PTO-2038 is attached.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17, 1.20(d) and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: December 20, 2004

By

Deborah H. Yellin
Reg. No. 45,904 for -

Melissa M. Hayworth
Registration No. 45,774



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re Patent Application of |) | |
| |) | |
| Kenneth C. CUNDY et al. |) | Group Art Unit: 1616 |
| |) | |
| Application No.: 09/974,768 |) | Examiner: Barbara P. Badio |
| |) | |
| Filed: October 9, 2001 |) | Confirmation No.: 6895 |
| |) | |
| For: BILE-ACID CONJUGATES FOR |) | |
| PROVIDING SUSTAINED |) | |
| SYSTEMIC CONCENTRATIONS |) | |
| OF DRUGS |) | |

RESPONSE TO OFFICE COMMUNICATION

Assistant Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

In complete and timely response to the Office Action of November 18, 2004, (December 18, 2004 and December 19, 2004 were a Saturday and Sunday, respectively), Applicants submit the following response.

In the Office Action, the Examiner requests that Applicants identify a group of compounds in accordance with the **exemplified** groups set forth in the previous Restriction Requirement dated July 16, 2004, or elect a group of compounds which are so similar within the same inventive concept and reduction to practice.

As discussed with Applicants' representative via telephone on Friday, August 13, 2004, the Examiner confirmed that the groups as set forth in the Restriction Requirement were **exemplary** and the Examiner noted that because the groups are exemplary, Applicants may define a group for examination not set forth among those specified in the Office Action. In accordance with the groups as set forth being exemplary and, thus, not limiting, and in an attempt to be fully responsive, Applicants have defined such a group for examination and elected it below. Applicants respectfully request that if the Examiner does not find Applicants' elected

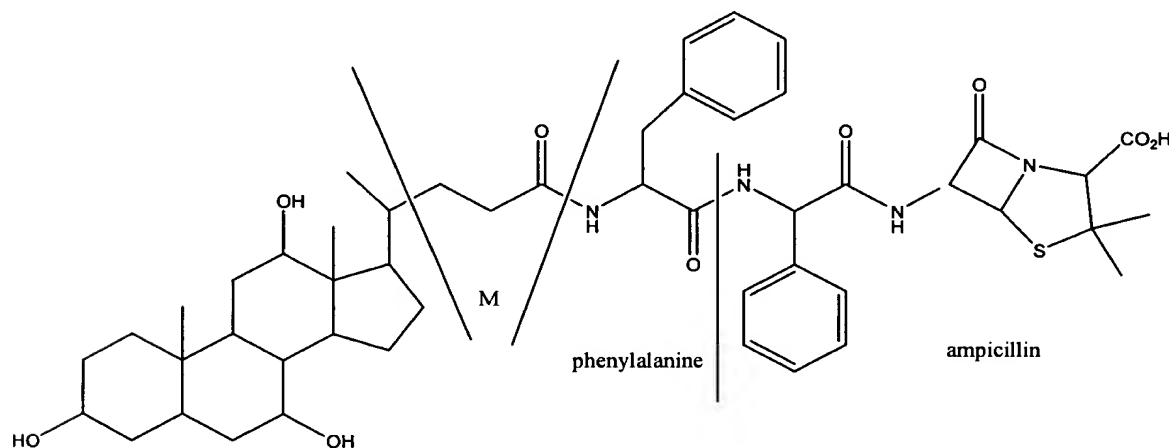
group acceptable, the Examiner define groups in a Restriction Requirement from which Applicants can choose that are in accordance with Applicants' invention and that one of which includes Applicants' elected compound.

Applicants believe that in paragraph 3 of the Office Action dated July 16, 2004 (on page 6), the Examiner was requiring that Applicants to elect a single disclosed species from under the elected Group for search purposes.

As in the previous response filed on August 16, 2004, Applicants respectfully traverse the restriction requirement as set forth in the Office Action, and thus, expressly reserve the right to Petition the Commissioner requesting removal thereof. Nevertheless, in order to comply with the requirements of 37 C.F.R. § 1.143, Applicants indicate below a provisional election of one group for examination and one species within the elected Group for purposes of searching.

Applicants maintain their election of species, with traverse, as set forth in the response filed on August 16, 2004. In the response filed on August 16, 2004, Applicants elected, with traverse, the following compound of formula I, for the purposes of searching in response to the election of species requirement.

Election of Species:



In the elected compound of formula I, X, R¹, and R² are hydroxy; Z is a group of the formula -M-Q^{x'}; M is -CH₂CH₂C(O)-; Q^{x'} is of the structure -I'_{i'}-J'_{j'}-D'-K'_{k'}-R_{40'}, wherein i' is 1 and j' and k' are zero, D' is ampicillin (as disclosed on page 82, lines 13-20), J' is derived from an α-amino acid (phenylalanine); and R_{40'} is -OH. Alpha amino acids are taught on page 33, line 18 –

page 34, line 2 and on page 35, lines 1-7. On page 35, line 6, phenylalanine is specifically disclosed as a suitable α -amino acid and phenylalanine is illustrated as a suitable α -amino acid in Figure 4. Ampicillin is specifically disclosed as a suitable drug D' on page 36, line 15.

Applicants note that in the Examiner-Initiated Interview Summary mailed September 29, 2003, Supervisory Patent Examiner Thurman K. Page indicated that Applicants' election of this compound would be considered proper by the U.S. Patent and Trademark Office.

Applicants maintain their election of the above compound, with traverse, in response to the election of species requirement.

In order to comply with the requirements of 37 C.F.R. § 1.143, Applicants indicate below an election of one group for examination, which group includes the above-elected compound.

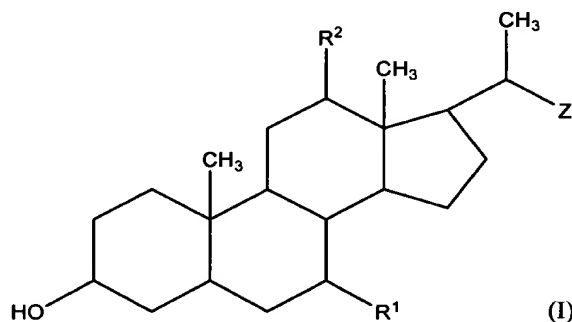
Applicants note that *none* of the exemplary groups as defined by the Examiner in the Office Actions of July 16, 2004 and November 18, 2004 include Applicants' elected compound. None of the exemplary groups as defined by the Examiner include D' being ampicillin, as in Applicants' elected compound. Applicants further note that as defined in the present application, I', J', and K' are preferably derived from α -amino acids and α -amino acids are taught on page 33, line 18 – page 34, line 2 and on page 35, lines 1-7. Applicants note that in the exemplary groups as defined by the Examiner, J' and K' are not present because j' and k' are zero. In addition, in the exemplary groups as defined by the Examiner, J' is $[\text{NR}_{50'}-(\text{CR}_{51'}-\text{CR}_{52'})_{a'}-(\text{CR}_{53'}-\text{CR}_{54'})_{b'}-\text{C}(\text{O})]$ wherein a' is 1 and b' is zero. However, the way in which the Examiner has chosen to define $\text{R}_{50'}$, $\text{R}_{51'}$, and $\text{R}_{52'}$ in the exemplary groups, naturally occurring α -amino acids are *not included* in any of the exemplary groups. Accordingly, the Examiner's exemplary groups are *not* in accordance with Applicants' invention and *do not* include Applicants' elected compound, which compound Applicants have consistently maintained as the elected compound since the response filed on *June 6, 2003*.

Accordingly, Applicants maintain their traversal of the restriction requirement and thus, expressly reserve the right to Petition the Commissioner requesting removal thereof. Applicants strongly assert that it is *improper* for the Office to refuse to examine that which Applicants regard as their invention and that it is *improper* for a Restriction Requirement to set forth groups that *do not include* that which Applicants regard as their invention. Therefore, Applicants

respectfully submit that the restriction requirement as set forth in the Office Action dated November 18, 2004 is improper.

In accordance with the groups as set forth being **exemplary** and, thus, not limiting, and in an attempt to be fully responsive, Applicants hereby propose and elect the following group for examination, which group includes the above compound elected in response to the election of species.

Elected Group: Claims 1, 3, 4, 6, 8, 9, and 23 (in part) drawn to compounds of formula (I) and compositions thereof:



wherein:

R^1 and R^2 are independently hydrogen or hydroxy; and

Z is a group $-M-Q^{x'}$, wherein M is $-\text{CH}_2\text{CH}_2\text{C}(\text{O})-$ and $Q^{x'}$ is of the formula $-\text{I}^{i'}-\text{J}^{j'}-\text{D}'-\text{K}^{k'}-\text{R}^{40'}$ wherein i' is 1; j' and k' are zero; $\text{I}^{i'}$ is selected from naturally occurring α -amino acid moieties, D' is ampicillin, and $\text{R}^{40'}$ is $-\text{OH}$.

Applicants respectfully request that if the Examiner does not find Applicants' elected group acceptable, the Examiner define groups in a Restriction Requirement from which Applicants can choose that are in accordance with Applicants' invention and that one of which includes Applicants' elected compound, which compound Applicants have consistently maintained as the elected compound since the response filed on June 6, 2003.

Applicants respectfully submit that the above-proposed elected group clearly exhibits unity of invention. With regard to a common utility, the compounds of proposed elected group use the bile acid transport system to provide sustained systemic concentration of orally delivered drugs (D'). With regard to a substantial structural feature, the compounds of the proposed elected group comprise a bile acid moiety, as illustrated above, linked to a drug (D'), which is

ampicillin. The bile acid moiety is joined with the drug (D'), which is ampicillin, by a group of the formula $-M-Q^x$, wherein M is $-\text{CH}_2\text{CH}_2\text{C}(\text{O})-$ and Q^x is of the formula $-\text{I}'_{i'}-\text{J}'_{j'}-\text{D}'-\text{K}'_{k'}-\text{R}^{40'}$ wherein i' is 1; j' and k' are zero; I' is selected from naturally occurring α -amino acid moieties, D' is ampicillin (as above) and $\text{R}^{40'}$ is $-\text{OH}$. Accordingly, Applicants respectfully submit that the compounds of the proposed elected group clearly evidence unity of invention.

In view of the proposed elected group and the policy regarding restriction of Markush-type claims as provided above, Applicants submit that it is improper for the Office to refuse to examine the proposed elected group, since the presently claimed subject matter clearly evidences unity of invention.

Applicants further respectfully submit the compounds of the proposed elected group are so closely related that a search and examination of the entire claim can be made without serious burden. Applicants note that a proper search can be made of the common backbone, as illustrated and discussed above.

If the restriction requirement is maintained as the Examiner has proposed, that which Applicants regard as their invention will never be examined, and Applicants will be forced to proceed with the filing of hundreds of applications, each consisting of generally the same disclosure, and each being subjected to essentially the same search. This process would place an unnecessary burden on both the Patent and Trademark Office and on the Applicants.

For the proposed elected group, it would be improper for the Office to refuse to examine that which Applicants regard as their invention when unity of invention exists. Accordingly, Applicants request reconsideration and withdrawal of restriction in view of their proposed elected group.

Conclusion

It is believed that claims 1, 3, 4, 6, 8, 9, and 23 are readable upon the elected species as defined above. Applicants have no intention of abandoning any non-elected subject matter and expressly reserve the right to file one or more continuation and/or divisional applications directed to the non-elected subject matter.

Applicants respectfully submit that their proposed a group for examination clearly evidences unity of invention. Applicants specifically reserve their right under 37 C.F.R. § 1.144

to petition the Commissioner from the present requirement for restriction if it is made final and from any further dissection by the Examiner of the Markush groups of the compounds of formula I.

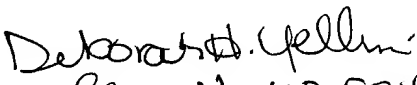
Again, Applicants respectfully request that if the Examiner does not find Applicants elected group acceptable, the Examiner define groups in a Restriction Requirement from which Applicants can choose that are in accordance with Applicants' invention and that one of which includes Applicants' elected compound.

In view of the foregoing remarks and proposed elected group, reconsideration of the claims is earnestly solicited. In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. 02-4800.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By  Reg. No. 45,904 for
Melissa M. Hayworth
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Dated: December 20, 2004